Research Article

Myelopathy in West Nile virus encephalitis: Report of a case and review of literature

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Context: In West Nile virus (WNV) encephalitis, polio-like illness has been reported but there is no report on acute transverse myelopathy.

Design, Setting and Participants: We report a patient with WNV myelopathy admitted in a tertiary care teaching hospital, India along with review of the literature.

Findings: A 34 year-old lady presented with fever, headache, diarrhea, seizure, bulbar weakness and quadriplegia for 20 days. Her encephalopathy, bulbar and upper limb weakness improved within few days but flaccid areflexic paraplegia persisted till 6 months with a horizontal sensory level at D3. Electromyography was suggestive of anterior horn cell involvement and somatosensory evoked potential was unrecordable. MRI revealed middle cerebellar peduncle, pons and whole of spinal cord involvement. We could get 11 articles with spinal cord involvement in WNV infection in the medical literature through PubMed search. Their clinical, MRI and electro-diagnostic findings and outcome have been discussed.

Conclusion/Clinical Relevance: Acute transverse myelitis may occur in WNV encephalitis and EMG may be helpful in confirming anterior horn cell involvement and predicting outcome.

Keywords: West Nile virus, Myelopathy, Transverse myelitis, Electromyography, MRI, Evoked potential, Prognosis

Introduction

West Nile virus (WNV) is an RNA virus, belonging to the family flavi-viridae and is spread by *Culex* mosquito. West Nile virus infection usually manifests with fever in equine animals and humans, and produces encephalitis. Surveillance immune serological testing within endemic areas suggest that only 20% of individuals affected by the virus develop systemic symptoms, and less than 1% develop neurological manifestations which include encephalitis, meningitis, anterior horn cell involvement and Guillain-Barre syndrome-like illness. Neurological involvement of WNV infection is associated with a mortality of 10–20%, and the survivors may have severe neurological deficits.[1]

West Nile virus is a neurotropic virus with a predilection to affect brainstem, cerebellum, and also anterior horn cells of spinal cord.[1,2] Sporadic and epidemic forms of WNV infection have been reported from Africa, Asia, Europe and United States.[2] In India, amongst the flavi-viridae infections, Japanese encephalitis and dengue are commoner.[3] West Nile virus infection has not been reported from Northern India. There is no report of long segment transverse myelitis due to WNV infection. In this communication, we report a patient with WNV transverse myelitis and review the literature.

Case report

A 34-year-old lady, village dweller of eastern Uttar Pradesh, India, presented with fever, pain abdomen and diarrhea for 20 days. On third day, she had headache and vomiting and on fifth day, she had rapidly progressive ascending quadriplegia with incontinence and slurring of speech. Following a generalized tonic-clonic seizure, she was drowsy for 24 hours. On 10th day, she was admitted in our hospital. On examination, her vitals were stable. She was conscious, comprehensive and communicable. Pupils were bilaterally equal and reactive. Ocular movements were normal but had bilateral gaze-evoked nystagmus. She had bilateral 7th, 9th and 10th palsy. There was flaccid quadriplegia of grade 0/5 power with generalized hyporeflexia. Joint position and vibration sensations were lost in all four limbs, and there was loss of pin prick and touch below

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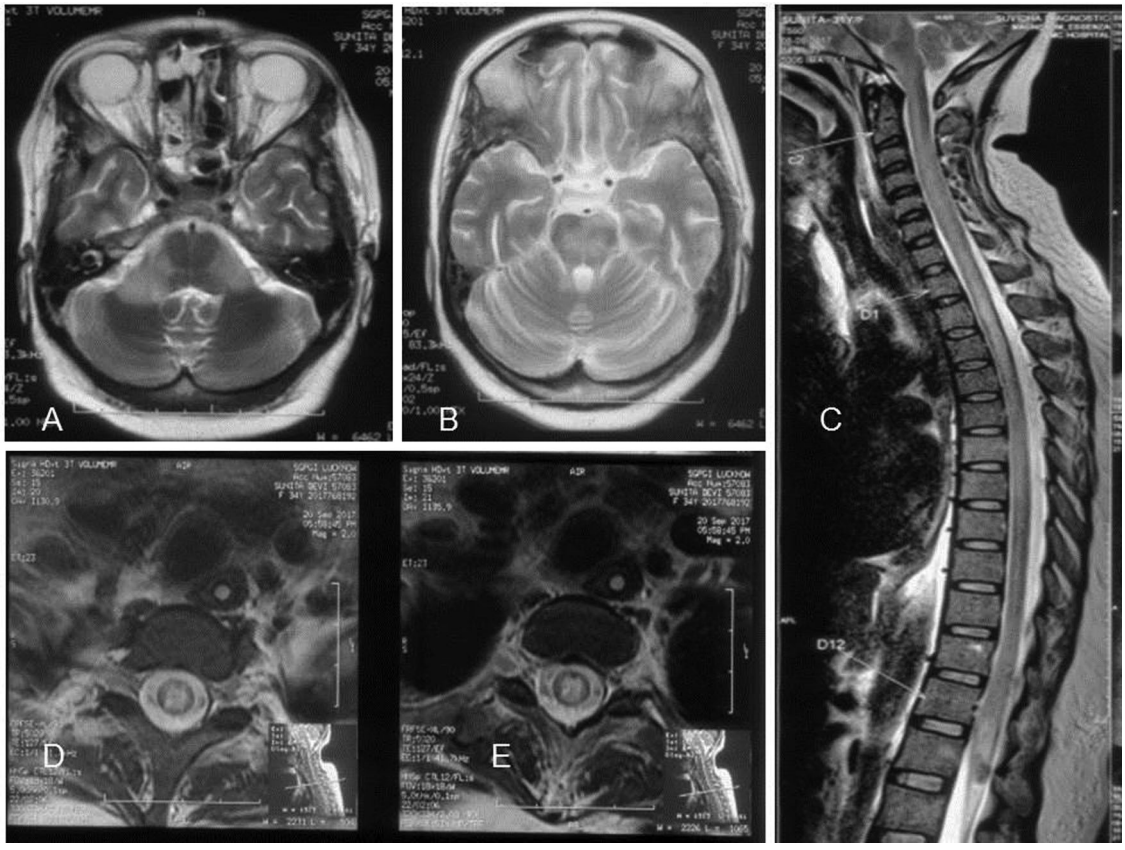

Figure 1 Cranio-spinal MRI in T2 sequence shows hyperintense signal changes in middle cerebellar peduncle bilaterally (A), central pons (B), whole of spinal cord (C). Axial sections of spinal cord (D & E) show hyper intense signal changes in the central part.

D3 spinal level. Light touch was impaired in C5 to D2. She was incontinent for bowel and bladder. Her American Spinal Injury Assessment (ASIA) score for motor was 0/100, light touch 12/112, pin prick 36/112, complete transection at D3 and ASIA Impairment Scale A. There was no organomegaly and cardiorespiratory examination was normal. Her total leucocyte count was 16400/mm^3, hemoglobin 12.4 gm/dl and ESR 36 mm at 1 hour, blood glucose 93 mg/dl, serum creatinine 0.38 mg/dl, creatine kinase 42 Unit/L, bilirubin 0.3 mg/dl, SGPT 175 unit/L, sodium 129 mg/dl and potassium 4.2 mg/dl. Vasculitic and thyroid profile, CRP, C3, C4, HIV serology, radiograph of chest and electrocardiogram were normal. Cerebrospinal fluid (CSF) analysis revealed 42 cells/mm^3 (neutrophils 55% and lymphocytes 45%), 149.3 mg/dl protein and 42 mg/dl glucose. CSF was negative for bacteria, acid-fast bacilli and fungus on smear and culture. CSF IgM ELISA for Japanese encephalitis virus and dengue virus were negative. Serum IgM ELISA for WNV was positive. MRI brain revealed T2 and FLAIR hyper intensity in middle cerebellar peduncles, pons, mid brain, and subcortical white matter. Spinal MRI revealed T2 hyper intensity extending from cervical to conus medullaris (Fig 1). There was no contrast enhancement. Electroencephalogram revealed theta slowing and was normal at one month. Peroneal nerve conduction was unrecordable but sural was normal (45 m/sec, 16 μv). Tibial somato-sensory evoked potential was unrecordable. Electromyography revealed fibrillations and sharp waves in tibialis anterior, vastus lateralis and gastrocnemius suggestive of anterior horn involvement. There was no recruitable motor unit potential. EMG of upper limb muscles was normal.

She was prescribed supportive care. At 6 months, her Mini Mental State Examination was 30, and bulbar and upper limb weakness were normalized. She was incontinent and bedridden due to flaccid, areflexic paraplegia (grade 0/5 power) with a sensory level at D3.

Discussion

Our patient had encephalomyelitis due to WNV infection and remained wheelchair bound due to necrotizing transverse myelopathy. Encephalitis was consistent with fever, headache, seizure, altered sensorium, CSF pleocytosis and cranial MRI showing brainstem involvement. The complete transection of spinal cord involvement was consistent with persistent flaccid paraplegia,

Table 1 Review of cases of WNV with myelitis.

Authors	Total cases (WNV Positive)	Other spinal cord changes	Myelopathy, MRI Findings	Electrophysiology	Outcome
1. Jonathan D. Fratkin, *et al.* (2004)[9]	193 (12 dead, 4 chosen for autopsy)	NA	All 4 Cervical+, Lumbar+	EMG showed denervation potentials	Autopsy finding
2. Jodie M. Burton *et al.* (2004)[10]	14 patients	NA	1 patients had T2W hyperintensity in thorasic segment	EMG showed Denervation potentials with neuropathic MUAPs. NCS: demyelinating with secondary axonal	NA
3. Pepperell C *et al.*[11] (2003)	64 patients	NA	2 patients; details of MRI not available.	EMG showed Denervation potentials on EMG	NA
4. Sejvar *et al.* (2003)[4]	16 patients	NA	3 had T2W hyperintensity with myelopathy; 2 showed enhancement of cauda equina	EMG showed Denervation potentials on EMG	Poor recovery at eight months
5. Jeha *et al.* (2003)[5]	11 patients	NA	3 had T2W hyperintensity in Cervical segment with Conus involvement	EMG showed Denervation potentials on EMG	
6. Ali. M *et al.* (2005)[13]	3 patients	1 patients had enhancement of cauda equina and lumbosacral roots	T2W hyperintensity in Conus medularis and thorasic segment.	ND	Poor recovery with Moderate-to-severe deficits
7. Petropoulou K A *et al.* (2005)[14]	3 patients	1 patients had enhancement of conus and nerve roots	2 had T2W hyperintensity Cervical cord lesion with Enhancement of conus and cauda		
8. equine	ND	Poor recovery			
9. Sejjvar *et al.* (2005)[16]	4 patients	NA	Involvement of anterior cord and ventral roots in cervical segment	EMG showed denervation potentials	NA
10. Maramattom BV *et al.*(2014)[15]	2 patients	NA	T2W hyperintensity in the cervico-thoracic cord	ND	NA
11. Al-Shekhlee and Katirji (2004)[16]	5 patients	NA	5 myelopathy, 1 patient had MRI, T2 hyperintensity of cervical gray mater	All showed fibrillations	1 improved, remaining had poor outcome
12. S. Saad *et al.* (2005)[17]	56		All myelopathy; 21 had spinal MRI: normal 13; cauda equina enhancement in 6 (2 conus), 1 C1–C7 T2 hyperintensity, 1anterior gray mater hyper intensity	Not specified	51 followed up; 11 died, 40 poor recovery (persistent weakness)

EMG, Electromyography; MRI, Magnetic resonance imaging; NA, not available; ND, not done; MUAPs, motor unit action potentials; NCS, Nerve conduction study.

electromyography showing evidence of anterior horn cell involvement (fibrillations and sharp waves), unrecordable tibial somatosensory findings and MRI revealing both horizontal and vertical extensive signal changes. About 80% of WNV infected individuals remain asymptomatic. Symptomatic illness develops 2–14 days following mosquito bite. About 20% of patients develop self-limited flu-like illness characterized by fever, myalgia, headache, gastrointestinal disturbance (20–30%) with a maculopapular rash in 25–50%. The CNS invasion of WNV is considered to be a part of hematological dissemination and WNV gains entry after disruption of blood-brain barrier by proinflammatory cytokines, tumor necrosis factor-alpha (TNF-α), interleukin-1beta (IL-1β), and macrophage migration inhibitory factor (MIF). In the brain, WNV can infect and replicate in various types of cells, including neurons, astrocytes, microglial cells and anterior horn cells.

Spinal cord involvement manifesting with polio-like illness has been reported in WNV infection both as a part of encephalitis and isolated polio-like illness[4–17] (Table 1). In a study, 3 out of 16 seropositive WNV encephalitis patients had flaccid weakness with rigidity, tremor and myoclonus.[4] West Nile virus myelopathy is usually asymmetrical, flaccid, areflexic, associated with bladder dysfunction but without a sensory deficit. Spinal MRI reveals signal changes in the anterior spinal cord and enhancement of cauda equina and anterior roots. Electromyography reveals evidence of anterior horn cell involvement.[1] Based on these findings, spinal cord manifestation in WNV infection is considered to be anterior horn cell damage. Al-Shekhlee and Kartirji reported paralytic polio-like illness in 5 patients due to WNV infection. Spinal MRI was done in one patient and revealed T2 hyper intensity of anterior gray mater. Electromyography in these patients was consistent with anterior horn cell involvement. One patient improved and the remaining 4 had a poor outcome.[16] Saad *et al.* reported 56 patients with acute flaccid weakness due to WNV infection including their 3 patients. The extent of paralysis ranged from single extremity to severe quadriplegia with bulbar weakness; 57% had quadriplegia, 4% triplegia, 13% paraplegia and 26% had monoplegia. Twenty-six percent of patients had cranial nerve palsy mainly facial diplegia, and 54% needed mechanical ventilation. Cranial MRI was non diagnostic. Spinal MRI was done in 21 patients and was abnormal in 8; 6 had cauda equina enhancement including conus in 2, one had T2 hyper intensity extending from C1–C7 and another had T2 hyper intensity of anterior gray mater. Fifty-one patients were followed up; 11 died and 40 had persistent weakness.[17] Polio-like illness has also been reported in other arbovirus infection such as Japanese encephalitis. In a study on 12 patients with JE, 7 had evidence of anterior horn cell involvement; focal reflex loss in 6, wasting in 7 and fibrillation and sharp waves in all the 7 patients. Lower motor neuron changes however were replaced by pyramidal or extrapyramidal signs at follow up.[18]

The longitudinal and horizontal extent of spinal MRI changes in our patient simulated MRI changes in acute transverse myelitis. Majority of reported WNV myelopathy patients including ours had poor prognosis, which may be due to extensive anterior horn cell involvement. In transverse myelitis, clinical (persistent areflexic flaccid weakness, wasting) and electromyographic evidences of anterior horn cell involvement (fibrillations, positive sharp waves) with few or no motor unit potential are associated with poor prognosis.[19] The recovery of upper limb weakness in our patient may be due to regression of cervical cord edema and the brunt of the myelopathic changes may be at the D3 level as sensory level corresponds to the severity.

This patient highlights the occurrence of myelopathy involving the sensory-motor system of the spinal cord which was evident on clinical, MRI and neurophysiological findings. Electromyography may be helpful in predicting long-term outcome of WNV encephalomyelitis.

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Disclaimer statements

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Competing of interest None.

Ethical Approval This study was approved by the Institutional Ethics Committee, SGPGIMS, Lucknow, India.

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